REMARKS

Claims 1 – 12, 15, 22, 28, 48 – 52 and 54 - 56 are pending in the application. Claims 3, 8 - 14, 16 – 21, 29 – 47, and 49 - 95 have been cancelled. Claims 1 – 7, 15, 22, 28 and 48 are under consideration. Claims 1, 15 and 48 have been amended. New claims 96 – 98 have been added. No new matter has been added by virtue of these amendments; support therefore can be found in throughout the specification and original claims of the application.

Any cancellation of the claims should in no way be construed as acquiescence to any of the Examiner's rejections and was done solely to expedite the prosecution of the application. Applicant reserves the right to pursue the claims as originally filed in this or a separate application(s).

Priority

The Examiner has acknowledged applicants claim for priority of International Application PCT/US04/040844 filed on 12/6/2004 and domestic priority under 35 USC 119(e) to US provisional application 60/527,615 filed on 12/5/2003.

Information Disclosure Statement

The Examiner has acknowledged and considered the IDS submitted on 5/22/2008.

Drawings

The Examiner has accepted the drawings submitted on 6/5/2006.

Claim Rejections 35 USC § 112, second paragraph

The Examiner has rejected claim 48 under 35 USC § 112, second paragraph, as allegedly failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Examiner indicates that "claim 48 is indefinite and vague in the recitation of 'a polypeptide according to claim 43'…because claim 43 is cancelled. It is not clear what the limitation of claim 48 is." (Office Action, p.4).

Claim 48 has been amended to recite dependency from claim 15. Accordingly, Applicants respectfully request that the rejection be withdrawn.

Claim Rejections 35 USC § 112, first paragraph

The Examiner has rejected claims 1, 2, 3 – 6, 7, 15, 22, 28 and 48 under 35 USC § 112, first paragraph, as allegedly failing to comply with the written description requirement. Applicants respectfully traverse the rejection.

Present claim 1 is directed to a purified and isolated catalytic domain from a β(1,4)-galactosyltransferase I consisting of SEQ ID NO: 6, and comprising a conservative amino acid exchange at amino acid position 344, wherein the catalytic domain catalyzes formation of galactose- ß(1,4)-N- acetylglucosamine bond in the presence of magnesium.

Present claim 15 is directed to a purified and isolated catalytic domain from a β(1,4)-galactosyltransferase I consisting of SEQ ID NO: 6, and comprising a conservative amino acid exchange at amino acid position 344, wherein the catalytic domain catalyzes formation of an N-acetylgalactosamine- β(1,4)-N-acetylglucosamine bond in the presence of magnesium.

The Examiner argues that the claims "are directed to any non-mutated or mutated catalytic domain from any galactosyltransferase I isolated from any source or man made having any structural feature comprising a conservative amino acid exchange at position 344 and 342 corresponding to SEQ ID NO: 6, which catalyses the formation of galactose- ß(1,4)-N- acetylglucosamine bond in the presence of magnesium" (Office Action, p.6).

Without acquiescing to the validity of the rejection and solely in the interest of advancing prosecution, Applicants have amended the claims to recite that the catalytic domain from a β(1,4)-galactosyltransferase I consists of SEQ ID NO: 6. As pointed out

by the Examiner at page 7 of the Office Action, the specification discloses the structure of SEQ ID NO: 6 to convey to one skilled in the art that the inventors had possession of the claimed invention.

Accordingly, Applicants respectfully request that the rejection be withdrawn.

The Examiner has rejected claims 1, 2, 3 – 6, 7, 15, 22, 28 and 48 under 35 USC § 112, first paragraph. The position is taken that the specification, while being enabling for mutated catalytic domains of a galactosyltransferase I of SEQ ID NO: 6, which catalyses formation of galactose-- β(1,4)-N-acetylglucosamine bond in the presence of magnesium, wherein the mutations are at positions 344, 342, 228 and 229 of a galactosyltransferase of SEQ ID NO: 6, does not reasonably provide enablement for any non-mutated or mutated catalytic domain from any galactosyltransferase I isolated from any source comprising a conservative amino acid exchange at position 344 and 342." (Office Action, p.7).

The present claims have been set forth above.

Without acquiescing to the validity of the rejection and solely in the interest of advancing prosecution, Applicants have amended the claims to recite a purified and isolated catalytic domain from a β(1,4)-galactosyltransferase I consisting of SEQ ID NO: 6, and comprising a conservative amino acid exchange at amino acid position 344, wherein the catalytic domain catalyzes formation of galactose- ß(1,4)-N-acetylglucosamine bond in the presence of magnesium.

The specification provides ample teaching to enable one skilled in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the present claims. Applicants describe at p. 10, beginning at line 10, catalytic domains that catalyze formation of a bond between a donor and an acceptor to form ß (galactose1,4)-N-acetylglucosamine bonds. Further, at page 11 of the application, Applicants provide an example of a specific exchange, M344H:

> In the presence of Mg^{2+}, the mutant, M344H-Gal-T1, exhibited 25% of the catalytic activity observed with the wild-

> type enzyme in the presence of Mn^{+}. It also has higher Km for the substrates. The crystal structures of M344H-Gal-T1 in complex with either UDP-Gal Mn^{+}+ or UDP-Gal Mg^{2+}, and the crystal structure of M344E-Gal-T1 in complex with UDP-Gal Mn^{2+}, have been determined at 2.3 ANG. resolutions. The structures show that the coordination stereochemistry of Mg^{2+} is quite similar to that of Mn^{2+}. Both His344 and Glu344 in the mutants exhibit stronger coordination bonds with the metal ion compared to Met344 in the wild-type enzyme. This strong metal-ion coordination in the mutants appears to reduce k_{cat} by interfering with the ability of the long flexible loop to undergo the required conformational changes during the catalytic cycle, but also by interfering with the formation of the transition state complex.

Further, Applicants teach the metal specificity of the mutants, where:

> …it was determined that the mutant M344H-Gal-T1, in the presence of Mn^{2+}, has only 1.5% of the wild-type enzyme activity. On the other hand, the mutant M344H-Gal-T1 exhibits 25% of its catalytic activity in the presence of an alkali metal ion, Mg^{2+}. In contrast, Mg^{2+} does not activate the wild-type enzyme. Although metal ions Mg^{2+} and Mn^{2+} bind to the mutant M344H-Gal-T1, their enzyme kinetics are different, indicating that the residue at position 344 and the appropriate metal ion play an important role in the conformational dynamics of the long loop in the catalytic mechanism of ß4Gal-T1.

Applicants also teach that amino acid residues that are involved with metal binding and that can be mutated can optionally include an additional mutation corresponding to amino acid position 342. For example, at p. 11, Applicants teach that "such a mutation may include exchange of cysteine at amino acid position 342 with threonine (C342T). However, other amino acids may be exchanged for cysteine that provide an active catalytic domain."

Accordingly, the teachings of the specification enable one of skill in the art to practice the full scope of the claimed invention. Applicants request that the rejection be reconsidered and withdrawn.

Claim Rejections 35 USC § 102(b)

The Examiner has rejected claims 1, 2, 7, 15 and 48 under 35 USC § 102 (b) as being allegedly anticipated by Vadaie et al. (Glycobiology, 2002 Oct; 12 (10): 589-97). Applicants respectfully traverse the rejection.

The present claims have been set forth above.

The Examiner argues that the Vadaie reference teaches a galactosyltransferase, which transfers galactose to its acceptor molecule in the presence of manganese, cobalt and magnesium." (Office Action, p. 12).

In order to anticipate a claim, each and every element of the claim must be found in the cited document. This is discussed in the Manual of Patent Examining Procedure, § 2131.

Nowhere does the Vadaie reference teach a purified and isolated catalytic domain from a β(1,4)-galactosyltransferase I consisting of SEQ ID NO: 6, and comprising a conservative amino acid exchange at amino acid position 344 of SEQ ID NO: 6, wherein the catalytic domain that catalyzes formation of galactose- ß(1,4)-N-acetylglucosamine bond in the presence of magnesium.

Applicants respectfully request that the foregoing rejection be withdrawn.

Early consideration and allowance of the application are earnestly solicited.

Respectfully submitted,

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